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This is a communication from the Patent and Trademark Office of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined. ☐ Responsive to communication filed on \_\_\_\_\_ ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ \_\_\_\_\_

Part II SUMMARY OF ACTION

1. ☒ Claims 1, 5-28 are pending in the application.  
Of the above, claims 5-13, 17-28 are withdrawn from consideration.
2. ☒ Claims 2-4 have been cancelled.
3. ☐ Claims \_\_\_\_\_ are allowed.
4. ☒ Claims 1, 14-16 are rejected.
5. ☐ Claims \_\_\_\_\_ are objected to.
6. ☒ Claims 1, 5-28 are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on \_\_\_\_\_, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received  
☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1 and 14-16, drawn to connective tissue growth factor (CTGF) fragments thereof and CTGF antibodies, classified in Class 530, subclass 399 and Class 424, subclass 85.8.

II. Claims 5-13, drawn to nucleotides, vectors and transformed or transfected cells, classified in Class 536, subclass 27, as well as Class 435, subclasses 320.1, 240.2 and 252.3.

III. Claims 17-19, drawn to a method of accelerating wound healing, classified in Class 514, subclass 12.

IV. Claims 20 and 21, drawn to a diagnostic assay, classified in Class 435, subclass 7.1.

V. Claims 22-28, drawn to a treatment method using a CTGF reactive agent, classification varies dependent upon the species.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as independent products, having different functions. Their independence is demonstrated by the fact that the products of Invention II may be used as nucleic acid hybridization probes rather than as templates for transcription and translation to generate the products of Invention I.

Inventions I and III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case, the product as claimed may be used as an antigen for the production of antibodies instead of as a therapeutic composition in a method of treatment.

Inventions I and V are also related as product and process of use. In the instant case, the product as claimed is useful as a diagnostic reagent instead of as a therapeutic composition in a method of treatment.

The remaining pairwise permutations of the above groups are unrelated, wherein each is not required, one for another.

Because these inventions are distinct for the reasons given above and have acquired a

separate status in the art because of their recognized divergent subject matter and/or different classification, restriction for examination purposes as indicated is proper.

Since this application is a continuation, not a divisional, filed under 37 C.F.R. 1.62, prosecution is being continued on the invention elected and prosecuted by applicants in the parent application, i.e. Group I, claims 1 and 14-16. See 1046 O.G. 2. Consequently, claims 5-13 and 17-28 stand withdrawn from further consideration by the Examiner, 37. C.F.R. 1.142(b), as being drawn to a nonelected invention. Election was made without traverse in Paper Number 4.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims

under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claim 1 is rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Matsuoka et al., or alternatively Campochiaro et al., or alternatively Shimokado et al.

Matsuoka et al. disclose the identification and purification of a PDGF-related protein of 34-36 kilodaltons (kD) from human wound fluid. The last paragraph of the first column, p. 4416 indicates that the peptides are biologically active as chemoattractants (e.g. chemotactic) and mitogens for connective tissue cells, and that they crossreact with anti-human PDGF IgG (antibodies). The paper does not specifically disclose that the protein is monomeric in nature, nor that it binds to PDGF receptors. However, as the disclosed 34-36 kD protein appears to be identical to the CTGF of the current application, these characteristics are considered to be inherent to the protein disclosed by Matsuoka et al.

Campochiaro et al. disclose the isolation of a PDGF-like protein from retinal pigment epithelial cells. Said protein has a relative mobility of 36-38 kD, is mitogenic and chemotactic, and binds to PDGF antibodies. The paper does not specifically disclose that the protein is monomeric in nature, nor that it binds to PDGF receptors. However, as the disclosed 36-38 kD protein appears to be identical to the CTGF of the current application, these characteristics are considered to be inherent to the protein disclosed by Campochiaro et al.

Shimokado et al. disclose the isolation of a PDGF-like protein of 37 kD, isolated from activated human alveolar and peritoneal macrophages. Said protein is mitogenic for connective tissue cells (p. 278), inhibited by anti-PDGF IgG (p.279) and competes for binding to PDGF receptors (paragraph bridging pages 279-280). The paper does not specifically disclose that the protein is monomeric in nature, nor that it has chemotactic properties. However, as the disclosed 37 kD protein appears to be identical to the CTGF of the current application, these characteristics are considered to be inherent to the protein disclosed by Shimokado et al.

Claim 1 is rejected under 35 U.S.C. § 102(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Ryseck et al.

Ryseck et al. disclose cloning and expression of fisp-12 from NIH 3T3 cells, a protein  
5 predicted to have 348 amino acids, with a predicted molecular weight of 37,792 daltons (p. 226, col. 2). A comparison of the amino acid sequences of fisp-12 and CTGF reveals only 13 discrepancies in the region between residues 86 and 392 (based on the numbering of Seq. ID No: 1). There is greater divergence in the region preceeding residue 86. However, Ryseck et al. identify this region as a signal sequence, which would have no effect on the activity of the  
10 protein. At the time of their disclosure, Ryseck et al. were unaware of the function of fisp-12, and made no mention of any ability to bind PDGF receptors. However, the degree of identity between the two proteins is such that the characteristics by which CTGF is claimed in Claim 1 are deemed by the Examiner to be inherent to fisp-12 in the absence of any evidence to the contrary.

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Claims 14-16 are rejected under 35 U.S.C. § 103 as being unpatentable over Matsuoka et al., or alternatively Campochiaro et al., or alternatively Shimokado et al., or alternatively Ryseck et al.

20 Having identified and purified the growth factor as demonstrated above, it would have been obvious to a person of ordinary skill in the art to generate antibodies specific to the growth factor and non-crossreactive with similar species for numerous reasons, including but not limited to a) to allow further study of the distribution and production of said growth factor, b) to aid in cloning said growth factor, c) to facilitate isolation of said growth factor from natural sources  
25 absent other related growth factors or e) for treatment of conditions relating to overproduction of the growth factor. All of the above applications would have been immediately obvious to a person of ordinary skill in the art, as would the techniques necessary to generate the specific antibodies of the invention.

This is a file-wrapper continuation of applicant's earlier application S.N. 07/752427. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds or art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See M.P.E.P. § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication should be directed to Lorraine Spector, Ph.D. at telephone number (703) 308-1793.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1, fax number (703)308-4227. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

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ROBERT J. HILL, JR.  
SUPERVISORY PATENT EXAMINER  
GROUP 1800